An Assessment of Pharmacist & Patient Knowledge of and Attitudes Toward Reporting Adverse Drug Reactions in Patients with Epilepsy

Submitted as part of Alyssa Chen's Undergraduate Honors Thesis

May 2008

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Note: This work has been presented by Alyssa at the:

- 2008 Ohio Pharmacists Association Research Forum – April 2008
  - *Podium presentation*
- 2008 OSU Denman Undergraduate Research Forum – May 2008
  - *Award winner in "Health Professions – Clinical" Category*
- 2008 OSU College of Pharmacy Research Day – May 2008
  - *Poster presentation*

ABSTRACT

Background: A survey was developed to gather information from both pharmacists and patients with epilepsy on the issue of antiepileptic drug formulation switching. This study looked at the patient-focused issues associated with switching among various forms of the same antiepileptic drug. This switching includes brand to generic, generic to brand and also generic to generic. Finding the right dose of the optimal treatment to prevent seizures in some patients with epilepsy is a complex and sometimes lengthy process. Formulation switching with antiepileptic drugs may have undesirable results such as an increase in seizure activity or an increase in adverse events. Education for the patient and the many healthcare professionals involved with the care of the patient with epilepsy is an important aspect of this issue. Since medication plays a major role in the treatment of epilepsy, pharmacists serve an important function in the health care of patients with this chronic disease. Pharmacists should take advantage of the opportunity to expand their roles in providing optimal care to their patients with epilepsy. Reporting adverse drug reactions with antiepileptic drug formulation switching through the FDA's Safety Information and Adverse Event Reporting Program (MedWatch, www.fda.gov/medwatch) is an example how this expansion can be achieved.

Purpose: The goal of this educational project was to assess patient and pharmacist knowledge of and attitude toward antiepileptic drug formulation switching and reporting of adverse drug reactions in patients with epilepsy.

Methods: We asked both pharmacists (n=500) and patients (n=250) to respond to a brief survey via the mail (pharmacists) or online (patients with epilepsy). The online survey on Zoomerang® was open for 6 weeks. Results: Data was obtained from 112 pharmacists and 82 patients (or parents of patients) with epilepsy. Nearly all respondents (>98%) agreed that finding the right dose of the right drug to prevent seizures can sometimes be difficult and take awhile. More than 85% of pharmacists and 92% of patients agreed that switching between forms of the same antiepileptic drugs may cause an increase in seizures or side effects. Nearly half (49%) of pharmacists knew of patients who have described problems when they have changed antiepileptic drug formulations. Similar numbers were reported by patients for themselves (41%) or a friend (48%). More than 4 out of 10 pharmacists (41%) and patients (45%) knew that situations involving patients experiencing problems with formulation switching should be reported as adverse drug events. Most pharmacists (75%), but less than half of patients (45%), knew that problems with switching between the same forms of antiepileptic drugs should be reported as adverse drug events. Most pharmacists (79%), but very few patients (6%), knew about the MEDWATCH program before the survey. While 27% of pharmacists reported using the MEDWATCH program, only one of them used it to report a patient experiencing problems with formulation switching. In our sample, only one patient out of 82 reported using the MEDWATCH program and this was for reporting problems with formulation switching. Both pharmacists and patients were more willing to learn about and use the MEDWATCH program after completing the survey.

Conclusion: We conclude that both pharmacists and patients with epilepsy are under-informed and under-involved with reporting adverse drug reactions.

BACKGROUND

Epilepsy is a common neurological problem affecting 1-2% of the United States population. Epilepsy has significant economic and social consequences. These can be minimized by optimal seizure control. Antiepileptic drugs (AEDs) are the mainstay of treatment in this chronic disease. Treatment goals for patients with epilepsy include the prevention of seizures, the reduction and/or prevention of adverse effects and drug interactions, improvement of quality of life and patient satisfaction.[1]

This project focuses on the patient-focused issues associated with switching among various forms of the same AEDs. This switching includes brand to generic, generic to brand and also generic to generic. Finding the right dose of the optimal treatment to prevent seizures in some patients with epilepsy is a complex and sometimes lengthy process. Formulation switching with AEDs can have undesirable results such as an increase in seizure activity or an increase in adverse events. Seizures have the potential to be life threatening, and can endanger the individual and others, particularly if they occur without warning or while the individual is engaged in the various activities of daily living. Hence, to risk the occurrence of seizures or adverse events by switching products is a matter of both public and individual safety. Though many exist now, a number of currently available AEDs will be available in generic formulations in the near future.

Because of the FDA's designation of drugs as bioequivalent, some believe that different formulations of the same product are entirely equivalent and interchangeable. This may be an accurate statement for many drug products on the market, but studies have documented that the FDA's acceptable therapeutic range for different formulations of AEDs may be too broad for some patients with epilepsy. Differences do exist and these differences may result in breakthrough seizures, unacceptable adverse drug reactions and, in turn, increased expense to the individual and to society.[2]

Of particular concern is the rate and extent of absorption (bioavailability) between different formulations. The plus 25% and minus 20% (80-125 rule) allowed by the FDA for variance in bioequivalence may result in lower concentrations with resultant seizures or higher concentrations and subsequent toxicity (Figures 1a & b). Many epilepsy patients do not tolerate such variability. Uncertainty about when seizure activity may occur is omnipresent in many patients' lives. Formulation switching can add to that uncertainty. It is our opinion that adverse drug reactions (either seizures or toxicity) from AED formulation switching go under-reported by both patients and healthcare professionals.

Education for the patient and the many healthcare professionals involved with the care of the patient with epilepsy is an important aspect of this issue. Since medication plays the major role in the treatment of epilepsy, pharmacists serve an important function in the health care of patients with this chronic disease. Pharmacists should take advantage of the opportunity to expand their roles in providing optimal care to their patients with epilepsy. Reporting adverse drug reactions with AED formulation switching through the FDA's Safety Information and Adverse Event Reporting Program (MedWatch, www.fda.gov/medwatch) is an example how this expansion can be achieved.

We developed a survey instrument to gather information from both pharmacists and patients on this issue. Our goal of this educational project was to assess both populations' knowledge of and attitude toward AED formulation switching and reporting of adverse drug reactions.

METHODS

This is a cross-sectional, descriptive study asking both pharmacists and patients to respond to a brief survey. Biomedical Institutional Review Board (IRB) approval was obtained and a waiver of consent granted.

Patient Survey

Patients or parents of patients with epilepsy were recruited from the Epilepsy Foundation of Central Ohio's database. A 21-question survey was uploaded onto Zoomerang® (www.zoomerang.com). The survey began with a cover letter defining switching forms of the same medication as, "1. Switching from a brand name to a generic drug, 2. Switching from a generic to a brand name drug, or 3. Switching from one generic to another generic drug." The survey was confidential and voluntary. The first 13 questions asked about their knowledge of and attitudes towards switching between forms of the same antiepileptic drugs and reporting adverse reactions when switching formulations. The last 8 questions were related to demographic information and the number of generic and brand name antiepileptic drugs they were currently using. Emails with a link to the Zoomerang survey were sent to 250 patients and the survey site was left open for 6 weeks.

Pharmacist Survey

Five-hundred Ohio pharmacists were randomly selected from the Ohio State Board of Pharmacy's database of registered pharmacists by randomly choosing 125 from each of the four community pharmacy practice types (independent community pharmacy, small chain, large chain, and clinic or medical center). The pharmacists were mailed a cover letter, a brief 19-question survey and a postage-paid return envelope. The survey was confidential and voluntary. The cover letter defined drug formulation switching and the potential for patients to experience problems. The first 12 questions dealt with their knowledge of and attitudes towards antiepileptic drug formulation switching. The last 7 questions collected demographic information. Surveys were collected over a six-week period of time.

Data Analysis

Descriptive statistics were used to characterize the demographic data and responses by population.

RESULTS

Data was obtained from 82 patients (or parents) with epilepsy and 112 pharmacists for a response rate of 33% and 22%, respectively. Some of the pharmacist surveys were not used due to them no longer living in Ohio, because they were no longer practicing pharmacy, they were not practicing pharmacy in one of our targeted community pharmacy areas or they came in past the 6 week deadline. Table 1 provides details on the respondent demographics from both populations.

Table 2 depicts the questions and responses from both patients and pharmacists. Nearly all respondents (>98%) agreed that finding the right dose of the right drug to prevent seizures can sometimes be difficult and take awhile. More than 85% of pharmacists and 92% of patients agreed that switching between forms of the same antiepileptic drugs may cause an increase in seizures or side effects.

As can be seen from Table 3, more than half (51%) of pharmacists knew of patients who have described problems when they have changed antiepileptic drug formulations. Similar numbers were reported by patients for themselves (43%) or someone they knew (48%). Of note, more than one-third of the patient respondents reported that this question did not apply to them.

More than 4 out of 10 pharmacists (41%) and patients (45%) knew that situations involving patients experiencing problems with formulation switching should be reported as adverse drug events. While most pharmacists (75%) knew that problems with switching between the same forms of antiepileptic drugs should be reported as adverse drug events, this was in contrast to less than half of patients (45%). Most pharmacists (79%), but very few patients (6%), knew about the MEDWATCH program before the survey. While 27% of pharmacists reported using the MEDWATCH program, only one of them used it to report a patient experiencing problems with formulation switching. In our sample, only one patient out of 82 reported using the MEDWATCH program and this was for reporting problems with formulation switching. Both pharmacists and patients were more willing to learn about and use the MEDWATCH program after completing the survey.

Table 4 summarizes the comments from by patients and pharmacists when asked if they did or did not see a role for themselves and why in reporting adverse reactions using MEDWATCH. As you can see, most of the respondents whom provided comments were positive in their responses, though some pharmacists gave reasons why they are not willing to use the MEDWATCH system.

Study Limitations

Our study is not without limitations. It was a cross-sectional study and thus did not track patients or pharmacists responses over time; they were asked their opinions just once. We did not validate the survey questions we developed. Our response rate for patients (33%) and pharmacists (22%) was less than optimal. For the patient population, we were limited to Central Ohio patients and those with internet access. For the pharmacists, we only sampled those from Ohio and thus our data may not be applicable to all pharmacists.

DISCUSSION

At present, no published data exists in the medical literature, specific to epilepsy, on the attitudes of patients and pharmacists on the issue of AED formulation switching. The high level of distrust among patients suggests their experiences with AED formulation switching have not been favorable.

Suggestions for adoption

This current survey points to areas where education about MEDWATCH could be targeted. It would be beneficial to engage patients with epilepsy (and their families and caregivers) about the importance of being involved in advocacy for themselves and others. Persons who are motivated to report their adverse experiences could be provided with resources explaining how to access MEDWATCH. The MEDWATCH program has both a web-based reporting system and a paper-based system. Health care professionals and pharmacists involved in epilepsy care could easily provide a pamphlet when they encounter patients who have had problems from AED formulation switching.

It is also plausible to think about utilizing advancing technology to allow pharmacists to spend less time reporting adverse drug events so they may be more willing to do it. For example, many hospitals have combined MEDWATCH with their own adverse event reporting system to make a more efficient process.

Pharmacists acknowledge their interest in helping patients as well as their professional role in reporting such events. Educational programs and continuing education credits could be provided to pharmacists. Overcoming barriers to reporting adverse events are likely the most important challenge. Pharmacists in busy practices are likely to have time limitations for reporting events. They may be able to prioritize events for reporting. They may also be able to encourage a greater role for patient involvement in reporting.

We conclude that both pharmacists and patients with epilepsy are under-informed and under-involved with reporting adverse drug reactions.

Acknowledgements: We would like to thank the patient and pharmacist respondents for their time and input. We are also grateful to the Ohio State Board of Pharmacy and the Epilepsy Foundation of Central Ohio for access to their databases and finally to The Ohio State University College of Pharmacy for providing scholarship monies for one of the authors (AC).

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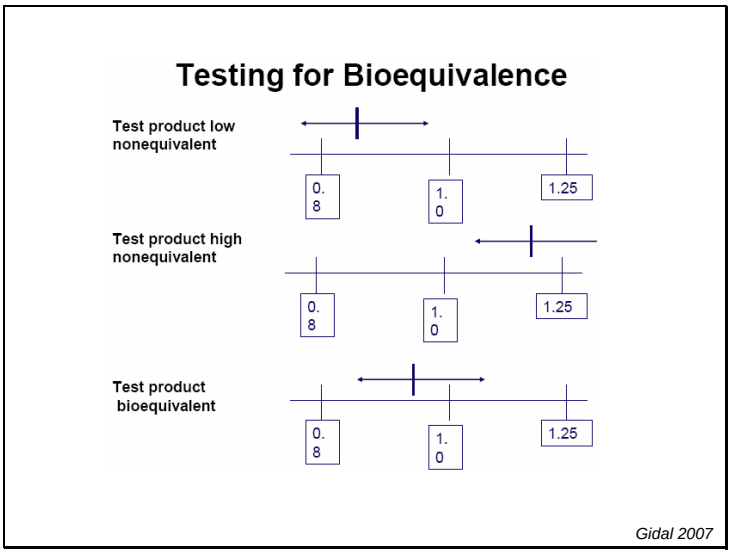

Figure 1a.

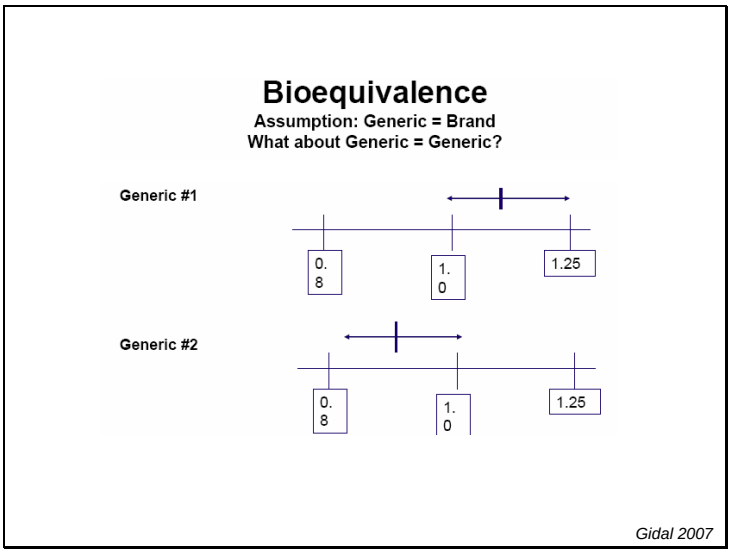

Figure 1b.

Table 1. Respondent Demographics

Patients (n=82)		Mean (SD)
Age of patient		27.1 (17.2)
Years taking antiepileptic drugs		12.86 (12.88)
Sex		
Men		38%
Women		57%
Not reported		5%
# Current AEDs	One	41%
	Two	38%
	Three or more	21%
# Current AEDs as Generic	Zero	70%
	One	18%
	Two	4%
	Three or more	3%
	Not sure	5%
# Current AEDs as Brand	Zero	10%
	One	44%
	Two	27%
	Three or more	10%
	Not sure	9%

Pharmacists (n=112)	Mean (SD)
Age (years)	47.3 (13.8)
Years in current practice setting	17.2 (12.3)
Patients with epilepsy seen per month	20.6 (26.3)
Sex	
Men	58%
Women	42%
Practice setting	
Independent Community Pharmacy	38%
Small Chain	17%
Large Chain	27%
Clinic/Medical Building	18%

SD = Standard Deviation
AED = Antiepileptic Drug
# = number

Table 2. Comparison of responses by population on questions that were asked of both populations

Survey Questions		Patients	Pharmacists
In general, formulation switching with most medications is safe.			
	Agree	38	96
	Disagree	62	4
Finding the right dose of the optimal treatment to prevent seizures in a patient with epilepsy can be a complex and sometimes lengthy process.			
	Agree	99	98
	Disagree	1	2
Switching between forms of the same antiepileptic drugs may cause an increase in seizures OR side effects.			
	Agree	96	87
	Disagree	4	13
Did you know that problems with switching between the same forms of antiepileptic drugs should be reported as adverse drug events?			
	Yes	47	41
	No	53	59
The FDA has a safety information and adverse event reporting program called MEDWATCH. It allows patients to report adverse drug events. Did you know about this program before today?			
	Yes	6	79
	No	94	21
Have you used the MEDWATCH program?			
	Yes	1	27
	No	99	73
Do you see a role for yourself in reporting adverse drug events through MEDWATCH?			
	Yes	59	88
	No	41	12
It is estimated that to take 20-40 minutes to fill out a MEDWATCH form. Does this fact deter you from using the program?			
	Yes	33	55
	No	67	45
After learning more about the MEDWATCH system, are you more or less willing to use it?			
	More	75	85
	Less	25	15
I am interested in learning more about switching between the same forms of antiepileptic drugs.			
	Yes	50	67
	No	50	33
I am interested in learning more about the MEDWATCH system.			
	Yes	74	68
	No	26	32

Table 3. Incidence of AED formulation switching problem reported by patients and pharmacists

Population	Question	Yes	No	Not Applicable
Patients (n=82)	I have experienced problems when switching between the same forms of my antiepileptic drug(s).	43%	19%	38%
	I know other patients that have experienced problems when switching between the same forms of their antiepileptic drugs.	48%	17%	35%
Pharmacists (n=112)	Patients with whom I have interacted have described problems when they have changed antiepileptic drug formulations.	51%	49%	

Table 4. Type and Frequency of comments provided from patients and pharmacists when asked why they Do or Do Not see a role for themselves in reporting adverse events through MEDWATCH

Patient Reasons	Frequency
Advocate for Themselves & Others / Desire to help others	25
Desire for Heightened Awareness / "Getting the Word Out"	2
Pharmacist Reasons if DID See a Role for Themselves	**Frequency**
Patient Safety / Increase Awareness of Problems	36
Pharmacist's Professional Responsibility / "Right thing to do"	16
Pharmacist's ready access to patients	6
Pharmacist Reasons if DID NOT See a Role for Themselves	**Frequency**
Too busy	2
Someone else's responsibility - not mine, should be patient or physician	2
Not familiar with MedWatch	2
Not enough patient information	2
Too lengthy	1
Too confusing	1